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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,108	10/08/2004	Ruediger Ridder	05033.0006.PCUS00	8587
27194	7590	02/22/2008		
HOWREY LLP C/O IP DOCKETING DEPARTMENT 2941 FAIRVIEW PARK DRIVE, SUITE 200 FALLS CHURCH, VA 22042-2924			EXAMINER AEDER, SEAN E	
			ART UNIT 1642	PAPER NUMBER
			MAIL DATE 02/22/2008	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<div>Application Number</div> <div></div>	Application/Control No.	Applicant(s)/Patent under Reexamination	
	10/511,108	RIDDER ET AL.	
	Examiner	Art Unit	
	SEAN E. AEDER	1642	

<b>Advisory Action</b> <b>Before the Filing of an Appeal Brief</b>	<b>Application No.</b> 10/511,108	<b>Applicant(s)</b> RIDDER ET AL.	
	<b>Examiner</b> SEAN E. AEDER	<b>Art Unit</b> 1642	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 16 January 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 2 months from the mailing date of the final rejection.  
 b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
 (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
 (b) ☐ They raise the issue of new matter (see NOTE below);  
 (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
 (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
 5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
 6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
 7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
 The status of the claim(s) is (or will be) as follows:  
 Claim(s) allowed: \_\_\_\_\_.  
 Claim(s) objected to: 2, 8, 23 and 27.  
 Claim(s) rejected: 1-3, 8, 11-17, 22-24 and 27.  
 Claim(s) withdrawn from consideration: 4 and 5.

#### AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
 9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
 10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
 12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_.  
 13. ☐ Other: \_\_\_\_\_.

/MISOOK YU/  
 Primary Examiner, Art Unit 1642

Continuation of 3. NOTE: The amendments to the claims and the arguments presented in the Reply of 1/16/08 would not persuasively overcome the rejection of claims 1-3, 8, 11-17 and 22-24 under 35 U.S.C. 103(a).

In the Reply of 1/16/08, Applicant argues that none of the prior art has disclosed a need to improve the specificity of p16 in a cytological testing procedure. Applicant further argues that Klaes et al does not recognize a problem that about 30% of metaplastic cases show some immunoreactivity with p16INK4a specific antibodies and that measuring p16INK4a alone cannot discriminate metaplasia from neoplasia in Pap smear. In regards to Solomon et al, Applicant argues that hc2 DNA testing cannot discriminate metaplastic cells from dysplastic cells or neoplastic cells. Applicant further argues that Solomon et al does not disclose testing for E7 protein. Applicant further states that, at the time of invention, there was no information on immunocytochemical testing of E7 in a uterine cervix sample. Applicant further indicates that there is no motivation to select p16 with E7. Applicant further argues that a person skilled in the art would have considered that p16 and E7 markers are redundant and that the combination of them would not render any additional information. Applicant further argues that Guccione et al does not cure an alleged deficiency of Klaes et al and Solomon et al.

The amendments to the claims and the arguments found in the Reply of 1/6/08 have been considered, but are not deemed persuasive. In regards to arguments based on motivation to detect both p16 and E7 protein, Applicant's arguments that motivation is required to recognize that the claimed method is to discriminate p16INK4a overexpressing metaplasia from p16INK4a overexpressing neoplasia or dysplasia are not deemed persuasive. Note that the preamble of claim 1, for example, is about the intended purpose or use of the claimed process and the wherein clause is about a natural phenomena that results from expression of two markers versus one marker. Unlike the recited manipulative method steps, the preamble and the wherein clause are not considered limitations to the claims. In regards to arguments that the references do not disclose testing for E7 "protein" and that there was no information on immunocytochemical testing of E7 in a uterine cervix sample at the time of invention, Von Knebel Doeberitz has been cited as teaching viral E7 protein is required to initiate cervical carcinogenesis. In regards to arguments that p16 and E7 would be considered redundant markers for cervical cancer and the combination of them would not render any additional information, as "redundant" markers one of skill in the art would be motivated to use both of them to avoid false-positive results.

Continuation of 11. does NOT place the application in condition for allowance because: The amendments to the claims have not been entered because they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.